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Nucleotide

Protein

Genome

Structure

PopSet

Taxonomy

OMIM

Bc

Search 

for



Limits

Preview/Index

History

Clipboard

Details

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Abstract



Sort



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Processing of engulfed apoptotic bodies yields T cell epitopes.

Bellone M, Iezzi G, Rovere P, Galati G, Ronchetti A, Protti MP, Davoust J, Rugarli C, Manfredi AA.

Divisione di Medicina II/Laboratorio di Immunologia del Tumori, Istituto Scientifico H San Raffaele and Universita di Milano, Italy. Bellonem@hsr.it

Programmed death via apoptosis is the metazoan physiologic mode of cell death. Apoptotic cells are recognized by scavenger phagocytes via a number of membrane receptors and engulfed. Thereafter, little is known of their fate, or that of phagocytes. Here, we have traced apoptotic cells upon their engulfment by macrophages. After 3 h, apoptotic cells were contained in discrete well-defined vacuoles. Upon overnight chase, several small vesicles, possibly originating from the fragmentation of original vacuoles, were evident all over the macrophage body. Furthermore, Ags were diffused in the cytosol of some cells, which raises the possibility that epitopes from engulfed apoptotic cells may associate with macrophage MHC class I molecules and be recognized by T lymphocytes. Indeed, Ag-specific CTLs recognize and specifically lyse syngeneic macrophages upon phagocytosis of MHC class I-positive or -negative apoptotic cells, provided that they contain the relevant Ags. Synthesis and membrane expression of class I molecules by macrophages, together with functional transporters associated with Ag presentation, were necessary for recognition and lysis. The indirect presentation of epitopes from engulfed apoptotic cells by scavenger Ag-presenting phagocytes may, in the absence of "danger" signals, have implications for the establishment of central and peripheral self-tolerance.

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